Pesticide/Fertilizer Mix II (California)

No CAS #
Swiss CD-1 mice; exposure via drinking water
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Started 11/30/88; Completed 1/11/92
NTIS #92140730/AS

Pesticide/fertilizer mixture (California) (PFM-C) is composed of six pesticides (aldicarb, atrazine, dibromochloropropane, 1,2-dichloropropane, ethylene dibromide, and simazine) and one fertilizer (ammonium nitrate) and represents a real-life mixture of groundwater contamination found in California (Heindel et al., Fundam Appl Toxicol 22:605–621 [1994]). PFM-C was tested in Swiss CD-1 mice, following the RACB protocol. The lowest dose was the median concentration found in California groundwater samples. Higher dose levels represented successively 10-fold concentration increases, so the dose levels used in this study have been termed 1×, 10×, and 100× dose levels. The highest dose was approximately 10% of the maximum concentration that was technically achievable. The bulk (98.5%) of the mixture was nitrate, the rest of the components totaled the remaining 1.5% by weight. Because this study was intended to simulate groundwater contamination, the route of exposure was drinking water. These concentrations produced calculated consumptions at the top dose of 311 µg/kg body weight of pesticides and 204 mg/kg of nitrate.

Water consumption by F_0 mice was increased only at week 14 in the continuous cohabitation phase (Task 2), and was unchanged at other times. Similarly, there were no effects on body weight during Task 2. There were no effects on any index of reproductive function in the first generation. This study is representative of the initial RACB design: if no reproductive effects were seen in the first generation, no necropsy data were collected, and the second generation was reared and tested for fertility effects. Unlike most previous RACB studies that were without effect on reproductive function, however, this study tested both the upper and middle concentrations for effects in the F_1 generation.

Consumption of the mixture did not affect the viability or body weight of the second generation before or after weaning. The only reproductive effects seen in the F_1 mating trial was a significant 3.5% decrease in pup weight adjusted for litter size, and a shortening (by 0.7 days, from 19.5 days) in the length of the gestation period. At necropsy, body weights of both sexes were unaffected by PFM-C exposure. Kidney weights showed an inverse dose response: the 10× dose males had a 12% increase in weight, while the 100× males had a nonsignificant 4% increase. In females, kidney weight in the middle and upper dose group was increased by 10 and 7%, respectively. There was an 11% decrease in seminal vesicle weight at 100× in the F_1s.

In summary, under the conditions of this study, this mixture of pesticides and a fertilizer was not a reproductive toxicant in Swiss CD-1 mice at these levels.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **92140730/as**
Chemical: **Pesticide/Fertilizer Mix (California)**
CAS#: **None**
Mode of exposure: **Drinking water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	1X	10X	100X
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	•	•	•
Water consumption	—, —	↑, ↑	—, —
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

F_1 generation — Dose concentration →	1X	10X	100X
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	—, —	—, —
Mortality	•	—, —	—, —
Adult body weight	•	—, —	—, —
Kidney weight[a]	•	↑, ↑	—, ↑
Liver weight[a]	•	—, —	—, —
Feed consumption	•	•	•
Water consumption	•	↑, ↑	↑, ↑
Clinical signs	•	—, —	—, —
Reproductive toxicity			
Fertility index	•	—	—
# live pups/litter; pup wt./litter	•	—, —	—, —
Absolute testis, epididymis weight[a]	•	—, —	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	—, —	—, ↓
Epidid. sperm parameters (#, motility, morphology)	•	—, —, —	—, —, —
Estrous cycle length	•	—	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	100X
NOAEL general toxicity:	100X
F_1 more sensitive than F_0?	No
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.